
miR-145 and miR-143 regulate smooth muscle cell fate and plasticity.

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Public Summary:

Scientific Abstract:

MicroRNAs (miRNAs) are regulators of myriad cellular events, but evidence for a single miRNA that can efficiently differentiate multipotent stem cells into a specific lineage or regulate direct reprogramming of cells into an alternative cell fate has been elusive. Here we show that miR-145 and miR-143 are co-transcribed in multipotent murine cardiac progenitors before becoming localized to smooth muscle cells, including neural crest stem-cell-derived vascular smooth muscle cells. miR-145 and miR-143 were direct transcriptional targets of serum response factor, myocardin and Nkx2-5 (NK2 transcription factor related, locus 5) and were downregulated in injured or atherosclerotic vessels containing proliferating, less differentiated smooth muscle cells. miR-145 was necessary for myocardin-induced reprogramming of adult fibroblasts into smooth muscle cells and sufficient to induce differentiation of multipotent neural crest stem cells into vascular smooth muscle. Furthermore, miR-145 and miR-143 cooperatively targeted a network of transcription factors, including Klf4 (Kruppel-like factor 4), myocardin and Elk-1 (ELK1, member of ETS oncogene family), to promote differentiation and repress proliferation of smooth muscle cells. These findings demonstrate that miR-145 can direct the smooth muscle fate and that miR-145 and miR-143 function to regulate the quiescent versus proliferative phenotype of smooth muscle cells.

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